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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/827,785	04/06/2001	Patrick Florent	B45096C1	7816

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EXAMINER	
LUCAS, ZACHARIAH	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 11/04/2003

11

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/827,785	FLORENT ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication app ars on the cov r sheet with th correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 August 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *9-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *10* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Status of the Claims

1. Claims 9-16 are pending and under consideration in the application.

2. A Final Rejection (the prior action) on claims 1-9 was mailed on May 27, 2003. In Response to that action, the Applicant filed a Request for Continued Examination (RCE) on August 11, 2003, in which claims 1-8 were cancelled, claim 9 was amended to read on a method of administering a booster vaccine to adults and adolescents, and new claims 19-16 were added. These new claims substantially mimic the limitations of cancelled claims 2-8, but differ from the previously rejected claims in that they now read on the method of claim 9 (rather than the product of cancelled claim 1), and therefore also include the additional limitations of amended claim 9.

3. Although the new rejections made in this action are in response to claim amendments, because the Office indicated that an RCE would be required in order for the amendments to be allowed into the case, the action is being made Non-Final.

Information Disclosure Statement

4. The information disclosure statement (IDS) submitted on August 13, 2003, is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the examiner.

5. It is noted that four of the references cited in that IDS have been crossed out. This is because these references have already been made of record by the Examiner in the action mailed on May 23, 2002. Thus, the citation of these references in the present IDS is redundant.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. **(Prior Rejection- Reformed and Maintained)** Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Feery et al, Med. J. Aust. 1:128-30 (Feery) in view of Edwards et al, Ped. Vol. 96 supp., pp. 548-57 (1995). Claim 1 has been cancelled from the Application. Claim 9 has been amended such that it now reads on the administration of a booster vaccine to adults and adolescents. The booster vaccine of claim 9 describes a .5 ml dose of a DTP comprising antigens as described as follows: D between 1-4 Lf, T does not exceed 10 Lf, PT is 2-10 μg, FHA is 2-10 μg, and 69K is between .5-3 μg per .5 ml dose.

In view of the claim amendments, the rejection is hereby reformed as follows: claims 9, 10, 15, an 16 are rejected as obvious over the teachings of Feery and Edwards as applied in the prior actions, further in view of Englund et al. (J Infect Dis 166: 1436-41), and in light of the teachings of Hewlett (Tokai J Exp Clin Med 13:125-28), and Keitel et al. (Semin Respir Infect 10: 51-57).

The Examiner agrees that the combined teachings of Feery and Edwards, alone, do not teach all of the limitations of the amended claim 9. The combined teachings render obvious the claimed formulation of the DTaP vaccine, but not its administration to adults. Further, while Feery teaches that a vaccine comprising 5 Lf of the tetanus antigen, and 2 LF of the diphtheria antigen, the vaccine is described as a primary vaccine, rather than as a booster vaccine. However, while the Examiner agrees that Edwards as Feery do not alone render obvious the method of amended claim 9, the Examiner does not agree that the art as a whole fails to teach or suggest the claimed method.

The Feery and Edwards references have been described in the prior actions. As indicated above, these references do not teach the use of the vaccine compositions in adults. However, Englund teaches that a vaccine composition meeting all of the vaccine limitations except for a higher dose of D, was immunogenic in, and produced few negative reactions in adults. Abstract, page 1440, left column. The reference further indicates that reduced antigen in the vaccine would retain suitable antigenicity, and have less potential for inducing local reactions. Page 1440, right column. As the combined teachings of Feery and Edwards ender obvious the claimed vaccine formulation (see, the prior action), and it would have been obvious to those in the art to use such a vaccine with lower dosages as the booster suggested by Englund. Therefore, the teachings of this reference, in combination with the teachings of Feery and Edwards as described in the prior action, render obvious the use of the claimed vaccine composition in adults.

However, it is noted that the references, while teaching that the composition may be used safely and effectively in adults, does not appear to provide any motivation for doing so, as there was previously no practice in the art to boost adult immunization against pertussis infection. The

further teachings of Hewlett and Keitel provide such motivation. Keitel teaches that adults may act as reservoirs for pertussis infection in children. Abstract. Further, each of Keitel and Hewlett note that there is an increasing incidence of pertussis infection in adults. Keitel, page 54; and Hewlett, abstract. Thus, in teaching that lack of adult immunization against pertussis leads both to increased incidence of child infection (with the adults as carriers), and that pertussis infection is becoming increasingly common in adults, in whom the effect of childhood vaccines is waning, the references provided motivation for those in the art to administer adults with a booster vaccine. Thus, cumulatively, the identified references render obvious the use of the claimed DTaP vaccine as a booster vaccine for previously immunized adults or adolescents.

Claim 9 also specifies that the claimed booster should be administered after prior administration of a higher dose vaccine. The application identifies as an example of a higher dose vaccine a vaccine known to the prior art. Further, the Edwards reference discloses other known vaccines with such higher dosages. It is further noted that, the Englund reference does not specify what prior vaccinations the recipients should have received. Neither the references, nor the specification, indicate that the efficacy of the booster vaccine is improved (or reduced) depending on the dosage of the primary vaccination. Because the art does not specify the primary vaccine, and because primary vaccines of higher dosages to the claimed booster were known in the art, it would have been obvious to those in the art to administer the identified booster to patients with any primary vaccine, including those who had received primary vaccines of higher dosages. Once it was established that the booster vaccine was safe and immunogenic, there would have been no reason for those in the art not to have a reasonable expectation of success in the use of the identified booster vaccine.

In addition to these teachings, it is noted that these two references also render obvious the use of the aluminum adjuvants of claim 15 and 16 in the DTaP vaccines obvious. Further, each of the three references teaches the inclusion of the additional antigens agglutinogens in the vaccine formulations. Thus, the references further render claim 11 obvious.

Applicant's citation of the CDC brochure in support of their arguments is noted. The brochure indicates that pertussis vaccines should not be administered to, and are not licensed for, people of over 7 years of age. However, in view of the teachings in the art cited above indicating that acellular pertussis vaccines are both effective and safe for use in populations of over seven years of age, the single citation by the Applicant, indicating that such vaccines are not licensed (and not that they are inoperative) is not found persuasive in demonstrating non-obviousness.

8. **(Prior Rejection- Reformed and Maintained)** Claims 1, 3-8, and 9 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Feery, and Edwards, and further in view of Petre et al, PCT/EP93/01276, and Eckhardt et al. U.S. Patent Number 5,895,655. As indicated above, claims 1 and 308 have been cancelled. However, claim 9 represents a method of using the vaccine composition that had been described in claim 1. The claim has been further described above. New claims 11-16 now incorporate the limitations of claims 3-8 into method claims depending from amended claim 9. In the RCE, the Applicant argued that the rejection indicated above should not be applied against the new claims depending from claim 9. The Applicant argued that it would not have been obvious to combine the teachings of Feery, Edwards, Petre, and Eckhardt because the references do not teach the administration of a DTaP vaccine to adults.

In view of the amendment to the claims, and for the reasons indicated above with reference to claims 9, 10, 15, and 16, the Examiner hereby reforms the rejection indicated above to read as follows: claims 9-16 are rejected as obvious over the teachings of Feery, Edwards, and Englund as applied against claims 9, 10, 15, and 16 above, further in view of Petre and Eckhardt, Inzana (U.S. Patent 5,429,818), and Prince et al. (Us Patent 4,695,454), and in light of the teachings of Hewlett and Keitel. The claims have been described above. Applicant's arguments in traversal of the rejection of claim 9 over the Feery, Edwards, Petre, and Eckhardt references are noted. However, the Examiner believes that the argument has been adequately responded to by the reformation of the rejection, and the discussion presented in support of the reformed rejection of claims 9, 10, 15, and 16.

The teachings of the references other than Inzana and Prince have been described either above, or in the prior action. These references teach the administration of the vaccine described in claim 9 to adults and adolescents, and teach that DTaP vaccines may be safely, and without loss of efficacy, combined with anti- Hib, polio, and hepatitis B (including those with HBsAg) vaccines. However, the references do not necessarily teach that DTaP vaccines intended for adults or adolescents may be combined with such other vaccines because there is no indication that adults need be vaccinated against these pathogens. Each of the Inzana and the Prince references provide such teachings. Prince, column 4, lines 20-25 (indicating that adults may be vaccinated against hepatitis B), and Inzana, column 1, lines 25-33 (teaching the same regarding the poliovirus). Thus, the references cumulatively indicate that those in the art would have been aware of the need for adult vaccinations against the pother listed pathogens, and that vaccine compositions against these pathogen may be safely and effectively combined with the DTaP

vaccine of claim 9. Thus, for substantially the same reasons as indicated against claims 3-8 in the prior action, and for the reasons above, the reformed rejection is maintained against claims 9-16.

9. **(New Rejection)** Claims 9 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of Shefer et al. (J Infect Dis 171: 1053-56) and Edwards et al. (JAMA 269: 53-56- Edwards II), and further in light of the teachings of Hewlett and Keitel as described above. Claim 9 has been described above.

Both Shefer and Edwards II are concerned with the immunization of adults against pertussis infection. Shefer, pages 1053, and 1056; and Edwards, page 53. These references, read in light of the teachings of the teachings of Hewlett and Keitel as described above, provide those in the art both suggestion and motivation to use DTaP vaccines as booster vaccines for adults and adolescents. Thus, the references render obvious the procedural aspects of the identified claim.

In addition to the suggestion of the references for the administration of booster vaccines to human populations greater than seven years of age, the Shefer and Edwards II references also disclose booster vaccine formulations that were found to be effective. The Chart below illustrates the dosages taught by Shefer on page 1054, and by Edwards II, on pages 53-54.

Antigen	Claim 9 Dosage	Edwards II- Full	Edwards II- Half	Edwards II- quarter	Shefer
D (Lf)	1-4	2	2	2	3.7
T (Lf)	<10	5	5	5	2.5
PT µg	2-5	3.2	1.6	0.8	1.6
69K µg	.5-3	1.6	0.8	0.4	0.8
FHA µg	2-10	34.4	17.2	8.6	17.2

As can be seen from the chart, neither Edwards II not Shefer teach any one vaccine that is completely with the claimed range. The two closest matches, the Shefer formulation and the

Edwards II half dosage formulation, each vary from the claimed formulation in the dosage level of the FHA and PT vaccine components. With respect to the FHA component, as the Edwards reference teaches that all of the dosage levels of this antigen were equally effective (page 54, rightmost column), it would have been obvious to those in the art to use any of these dosages. As those in the vaccine art tend to use the smallest effective dose, it would therefore have been obvious for those in the art to use a vaccine comprising the 8.6 μg FHA dosage in the booster vaccines.

With respect to the PT dosage, while those in the art would normally prefer the lowest dosage, in the present case, the Edwards II reference also teaches that only the full PT dosage was effective at inducing a boosting response. Page 54, rightmost column, second paragraph. Thus, while both references teach that all of the vaccine formulations are safe, the Englund reference provides both a suggestion and motivation for using only the PT dosage that falls within the claimed range. In view of the above, the combined teachings of the identified references render the method of claim 9 obvious.

Each of the Edwards II and the Shefer references further teaches the booster vaccines also comprise another antigen- pertussis agglutinogens. Edwards II, page 53; and Shefer, page 1054. As the references teach the inclusion of this additional antigen in the booster, the references also render obvious the method of claim 11, which requires the inclusion of an additional antigen in the administered booster vaccine.

10. **(New Rejection)** Claims 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shefer, Edwards II, Hewlett, and Keitel as applied to claims 9 and 11 above,

and further in view of Edwards. The teachings of the claims and the references have been described at least in part above. As was indicated in the prior action, Edwards also teaches that the various DTP vaccines disclosed therein contain various aluminum adjuvants. Page 550. It would therefore have been obvious to those in the art that such adjuvants could also be incorporated into the vaccines suggested by the combination of the Shefer and Edwards II references.

11. **(New Rejection)** Claims 9, and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shefer, Edwards II, Edwards, and in light of Hewlett, and Keitel as applied to claims 9, 11, 15 and 16 above, and further in view of Petre and Eckhardt, Inzana, and Prince as applied above. This rejection is primarily directed against claims 11-14 as described above. The present combination of the Shefer, Edwards, and Edwards II teachings with those of Petre, Eckhardt, Inzana, and Prince is made for substantially the same reasons as indicated above regarding the teachings of Feery, Edwards, and Englund, with Petre and Eckhardt, Inzana, and Prince as indicated above. Thus, because these references teach the use of the claimed DTaP vaccine with adults, suggest the combination of the DTaP vaccine with other vaccines, and because the other vaccines are known to be administered to adults, the references render the methods of claims 9, and 11-16 obvious.

Conclusion

12. No claims are allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
October 23, 2003

JAMES HOUSEL 11/3/03
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